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A Guide to AIDS Research and Counseling

Converging Epidemics: HIV and Hepatitis C Coinfection

Heather Lusk

Hepatitis C is the most common chronic blood-borne disease in the United States and the most common clinically significant coinfection in people living with HIV. Fifteen to 45 percent of people infected with hepatitis C will clear the hepatitis C virus on their own. The remainder live with hepatitis C for decades, resulting in liver disease and making hepatitis C a leading cause of hospitalization and death among people with HIV in the United States.

For these reasons, the Centers for Disease Control and Prevention recommends routine hepatitis C screening for people with HIV.¹ This article reviews the epidemiology of HIV–hepatitis C coinfection, and the transmission and prevention, manifestation, and treatment of hepatitis C infection among HIV-positive people.

Globally, the World Health Organization estimates that there are more than 170 million people living with hepatitis C and more than 40 million living with HIV. Millions of people worldwide are coinfecting with both infections. According to the CDC, as many as 4 million people in the United States have been infected with hepatitis C and 1.2 million have HIV: between 250,000 and 300,000 people live with both conditions. This means that as many as 30 percent of all people with HIV must deal with the challenges of hepatitis C coinfection.

Hepatitis C Transmission and Prevention

Hepatitis C is transmitted primarily through direct blood-to-blood contact, with more than 60 percent of all new infections occurring in people who inject drugs. Other key routes of transmission are blood and blood product transfusions prior to 1992, health care occupational expo-

sures to infected blood, and transmission from mother-to-child. Other activities such as having sex with someone with hepatitis C, getting unsterile tattoos and piercings, snorting drugs, and sharing personal items that have blood on them have been linked to transmission and are categorized as having low or unknown risk.² Unlike HIV, hepatitis C can survive outside the body for up to four days, explaining why some activities that cannot transmit HIV may transmit hepatitis C. While small amounts of hepatitis C virus have been found in other bodily fluids, there is little evidence that these fluids can transmit hepatitis C without the presence of blood in them.

It is a common assumption that hepatitis C is a sexually transmitted disease like HIV. However, research has shown that hepatitis C is not efficiently spread through sex. In the United States, the estimated prevalence of hepatitis C is 2 percent to 3 percent among partners of persons living with hepatitis C who are in long-term monogamous relationships, but it rises to between 4 percent and 6 percent among people with multiple sex partners, sex workers, men who have sex with men, and people at risk for sexually transmitted diseases (STDs).³ Sexual transmission of hepatitis C may be increased by the presence of STDs, trauma, and blood during sexual activity. While studies of sexual transmission consistently find a low prevalence of hepatitis C among heterosexual monogamous partners of people with hepatitis C, there needs to be more research into the factors that increase the likelihood of sexual transmission of hepatitis C.

Impact of HIV on Hepatitis C Transmission

Several recent studies have shown an increase in cases of acute or newly acquired hepatitis C in men living with HIV. During the 2006 Conference on Retroviruses and Opportunistic Infections, two sets of researchers—one from London and one from Amsterdam—reported on samples of HIV-positive men who have sex with men.

Editorial: Coping with Coinfection

Michelle Cataldo, LCSW, Clinical Editor

As many people with HIV know all too well, hepatitis C is the most medically significant coinfection they face and a leading cause of hospitalization and death for those living with both illnesses. While, for some people, HIV has indeed become a “chronic, manageable illness,” this phrase obscures both the wearing effect of chronic illness and the complexity of managing a “manageable” disease. Hepatitis C doubles these challenges.

People with HIV depend on antiviral medications to sustain their health, and hepatitis C threatens their abilities to metabolize these medications, further limiting treatment choices. Hepatitis

C, itself, is correlated with cognitive deficits and diminished quality of life and, ironically, its treatment with interferon often leads to depressive symptoms.

In this issue of *FOCUS*, authors Heather Lusk and Charles Raison each mix these stark realities with the good news about viral detection, and the hope of effective prevention, treatment, and disease resolution. In fact, as Lusk reports, a significant percentage of those exposed to hepatitis C defeat the virus without treatment. For those who do not, drug treatment can improve liver health and delay the worst effects of hepatitis C for decades. While treatment is diffi-

cult, adding to the burdens coinfecting people already face, recent improvements have made it easier for people with hepatitis C to maintain their treatment regimens.

Mental health providers can ease some of these burdens by recognizing the significant effects of hepatitis C and its treatment on the quality of life of their clients. They can also be alert to signs of depression and cognitive impairment and collaborate with medical professionals around treatment of these symptoms. As Raison points out, antidepressant treatment, especially prior to starting interferon, is successful in warding off depressive symptoms. Finally, clinicians can help clients make choices about their self-care—including substance use—and can improve their success and cushion the bumpy ride of coinfection.

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2. Centers for Disease Control and Prevention. *Recommendations for prevention and control of hepatitis C virus (HCV) infection and HCV-related chronic disease*. Morbidity and Mortality Weekly Report. 1998; 47(RR-19): 1–39.

They concluded that trauma to the anal mucous membranes, caused by activities such as fisting, was correlated with hepatitis C infection. Further, men who acquired hepatitis C were more likely to have sex while high (in the London study) and to have a concurrent STD infection (in the Amsterdam study). Additional studies in France and Switzerland have found similar evidence of increased risk of sexual transmission of hepatitis C among HIV-positive men who have sex with men,^{4,5} and several smaller studies have hinted at an increased risk for HIV-positive women through unprotected vaginal sex.

Researchers have also found higher mother-to-child hepatitis C transmission rates in mothers with HIV (19 percent) than in mothers without HIV (4 percent to 6 percent).⁶ While hepatitis C treatment during pregnancy is not recommended, HIV treatment during pregnancy may decrease the chance of hepatitis C transmission to the fetus.⁶

Hepatitis C Antibody and RNA Testing

As mentioned above, the CDC recommends hepatitis C screening for people with HIV. Unlike an HIV-positive result, a hepatitis C-positive result does not necessarily mean a person is currently infected with hepatitis C. While most hepatitis C-positive results — 55 percent to 85 percent—indicate a current infection, 15 percent to 45 percent of people who test positive for hepatitis C antibod-

ies have already “cleared” the virus and are no longer infected with hepatitis C. For these people, a hepatitis C-positive result indicates a prior, not current, infection with hepatitis C.

For this reason, hepatitis C antibody-positive results should be followed with a hepatitis C RNA test to determine if the hepatitis C virus is still present. Some experts recommend that some HIV-positive people who have tested hepatitis C antibody-negative should also be screened for hepatitis C RNA. These individuals—people with advanced HIV—may not be able to generate a sufficient immune response to produce a detectable level of hepatitis C antibodies and may test hepatitis C-negative even though they are infected. Clinicians should use the RNA test, which detects the virus itself, for HIV-positive people whose histories suggest a high likelihood of having been infected with hepatitis C and for those with an unexplained elevation of liver enzymes. Likewise, since a robust immune response is necessary to overcome hepatitis C, people with HIV may be less likely to clear hepatitis C and, as a result, may have higher rates of chronic infection.

Once hepatitis C RNA has been detected, clinicians use a series of blood tests to gauge liver function and possible liver damage. Since the levels of these biochemical and liver function markers fluctuate, most experts agree that a liver biopsy is the gold standard to assess level of liver damage. Two additional

**The fat molecule, called polyethylene glycol, is abbreviated "peg."*

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tests, a quantitative hepatitis C RNA and a hepatitis C genotype test, may be indicated when a person is considering hepatitis C treatment. Hepatitis C viral load does not correlate with hepatitis C disease progression, but hepatitis C viral load is used to determine hepatitis C drug treatment response.

Guidelines for Responding to Coinfection

In 2005, two prestigious bodies published the first recommendations specifically designed to support providers in effectively treating the complexities of HIV–hepatitis C coinfection. First, after a study found almost 40 percent of U.S. veterans being treated for HIV were also coinfecting with hepatitis C, the U.S. Veterans Administration released guidelines on the management and treatment of hepatitis C in people living with HIV.⁷ Second, the European Association for the Study of the Liver (EASL) convened the First European Consensus Conference on the Treatment of Chronic Hepatitis C and B in HIV Co-Infected Patients. The resulting consensus statement summarized the current evidence on coinfection and its treatment as well as the impact of HIV on the acceleration of hepatitis C-associated liver disease progression. The statement documented increased rates of liver decompensation, cirrhosis, hepatocellular carcinoma, and liver-related mortality for coinfecting people compared to people with hepatitis C alone.⁸

Research has consistently demonstrated this impact of HIV on hepatitis C disease progression, but results have been less consistent regarding the impact of hepatitis C on HIV disease. A few studies have found lower CD4+ cell counts and a more rapid progression to AIDS in coinfecting people when compared to those with HIV alone. Many studies, however, have found no difference in immune system status, HIV disease progression, and response to HIV antiviral treatment between the two groups.

The European Consensus statement recommends treating HIV in people coinfecting with hepatitis C the same as treating HIV infection alone, following current guidelines for HIV antiviral treatment. However, the statement also suggests some exceptions. For people newly infected with HIV and for those with high CD4+ cell counts and low HIV viral load, hepatitis C treatment may be appropriate prior to HIV antiviral treatment. Further, since coinfecting people with CD4+ cell counts of less than 200 have a reduced hepatitis C treatment response, clinicians should seek to stabilize CD4+ cell counts prior to hepatitis C treatment. HIV antiviral medications such as nevirapine have been linked with liver toxicity, and some medica-

tions such as didanosine are contraindicated with hepatitis C treatment.

Since HIV antiviral treatment can be toxic to people with liver disease, coinfecting people need careful management and observation in order to balance HIV treatment with the goal of minimizing liver-related side effects. Further, patients with stabilized HIV should consider treatment in hopes of eradicating hepatitis C and increasing both their liver health and the liver's capacity to manage HIV treatment.

Treating Hepatitis C Itself

The goal of hepatitis C treatment is to achieve a "sustained virologic response," indicated by undetectable levels of hepatitis C RNA for 24 weeks after treatment is completed. However, even without this response, treatment can lead to improvements in liver health and function and delays in liver disease progression. There is also evidence—but no published formal guidelines recommending this—that treating hepatitis C in the acute stage may prevent the development of chronic hepatitis C infection.

Clinical opinions about who is a good candidate for treatment vary, and many people with a history of drug and alcohol use have been denied hepatitis C treatment without at least six months of sobriety. The latest NIH Consensus Statement on the Management of Hepatitis C, however, recommends that "active injection drug use in and of itself [should] not be used to exclude such patients from [hepatitis C] antiviral therapy." It is important to note that a recent study demonstrates that very few active drug users have access to treatment for hepatitis C.⁹

The standard of care for hepatitis C treatment is injectable pegylated interferon combined with the antiviral drug ribavirin for between 24 and 48 weeks. Pegylation, a process by which the interferon is encased in a fat molecule, slows the metabolism of the drug and allows for fewer injections.* It is general practice that people who are coinfecting with HIV and hepatitis C finish the full 48-week course of treatment. More physicians are relying upon measures of "early virological response" to predict treatment response, since evidence shows that without a significant drop in hepatitis C viral load after 12 weeks of treatment, there is very little chance of attaining sustained virologic response even after 48 weeks. Without this early response, many physicians are stopping treatment.

Being able to gauge the value of treatment is particularly important since hepatitis C treatment has many side effects, including flu-like symptoms, depression, anemia,

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fatigue, aches and pains, diarrhea, hair loss, nausea, and sleep and eating disruptions. Anemia, caused by ribavirin, is of particular concern for people living with HIV. Side effect management is key to treatment adherence, which requires taking at least 80 percent of medications 80 percent of the time. Side effect management may include prescribing additional drugs for depression, anemia, or other effects of the medication. While interferon remains the core of treatment, researchers are seeking alternative antiviral drugs in order to reduce side effects.

In February 2005, based on the results of the AIDS Pegsys Ribavirin International Coinfection Trial (APRICOT),¹⁰ the U.S. Food and Drug Administration approved the first and only combination drug treatment for hepatitis C in people with HIV: Roche Pharmaceuticals' Pegsys (pegylated interferon alfa-2a) and Copegus (ribavirin). Prior to FDA approval, clinicians had prescribed these drugs "off label," that is, legally but without FDA sanction. There continues to be off-label use of other brands of pegylated interferon with ribavirin that are not specifically indicated for coinfection. The APRICOT study, which was conducted in over 19 countries, found an overall sustained virologic response rate of 40 percent in coinfecting patients taking Pegsys/Copegus. These results varied significantly by hepatitis C genotype: only 29 percent of patients with genotype 1 had a sustained virologic response compared with 62 percent of those with genotype 2 or 3. While these response rates were lower than in people who have hepatitis C alone, this study nonetheless demonstrated that hepatitis C can be successfully treated in people with HIV.

Two other large studies on hepatitis C treatment in coinfecting people (ACTG A5071 and RIBAVIC) also confirmed that pegylated interferon with ribavirin is more effective than standard interferon alone. Many states have included hepatitis C treatment on their AIDS Drug Assistance Program (ADAP) formularies.

Other Hepatitis Treatment Approaches

In addition to drug-based therapies, treatment guidelines recommend that people who are coinfecting be vaccinated against hepatitis A and hepatitis B to prevent additional liver damage. Since vaccine response is linked to high CD4+ cell count, people with HIV should undergo post-vaccination testing to ensure hepatitis A and B immunity. Some experts also recommend screening for chronic hepatitis B virus because of the higher rate of chronicity among people with HIV. As with hepatitis C disease progression, hepatitis B progression seems to be more accelerated in people coinfecting with HIV than in people with hepatitis B alone. Currently, the FDA has approved no hepatitis B medication specifically for people with HIV, but some HIV treatment medications, such as lamivudine and tenofovir, also are effective against hepatitis B.

Because of alcohol's toxic effects on the liver, people with hepatitis C should limit alcohol consumption. This is particularly true for HIV-positive people, because of the liver toxicities associated with HIV antiviral treatment. Limiting additional liver toxins such as excess medications or vitamins, eating a low-fat and balanced diet, getting moderate exercise, and drinking water will all support liver function and health.

Conclusion

HIV providers should address viral hepatitis with all their clients with HIV in order to help prevent the transmission of all forms of viral hepatitis. People who are coinfecting with HIV and hepatitis B or C may need to work with specialists familiar with both diseases to support the complex medical management of coinfection. Recent research has given hope to many that through awareness and education, hepatitis C-related liver disease does not have to be one of the leading causes of death among people living with HIV.

Clearinghouse: Hepatitis C and HIV

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The Effects of Hepatitis C and its Treatment on Mental Health

Charles Raison, MD

Thirty percent to 60 percent of people on hepatitis C treatment will develop clinically significant depression.

Long before the disease had a specific name, hepatitis C was infamous for its often lethal signature on the liver, marking it as a

primary cause of liver failure, the chief risk factor for liver cancer, and the pre-eminent reason for liver transplantation.¹ In combination with HIV, hepatitis C takes an especially virulent turn.

These consequences—while dire—represent only the tip of the iceberg in terms of the overall health burden of hepatitis C. Hepatitis C also significantly impairs the quality of life of infected individuals.² In fact, more than two-thirds of the health care costs associated with hepatitis C derive from its negative impact on quality of life and the resulting inability of people with hepatitis C to function.² Fortunately, recent data indicate that treatment offers hope for improving many of these behavioral symptoms.³

Quality of Life

When compared to control subjects without hepatitis C, subjects with hepatitis C demonstrate declines in all domains relevant to quality of life, including physical and emotional role functioning, social functioning, and overall physical health status.² Once cirrhosis has developed, it is clear that impaired liver functioning contributes to these losses.² In patients without cirrhosis, however, hepatitis C-related quality of life impairments do not clearly correlate to either liver functioning or pathology.²

Rather, diminished quality of life appears to be more closely related to the high prevalence of neurobehavioral symptoms such as depression, anxiety, fatigue, and cognitive disturbances—decreased concentration, attention, and memory—observed in this population.⁴ In this regard, hepatitis C is not unique: such symptoms account for much of the diminished quality of life associated with medical illness, in general.

While people with hepatitis C suffer a disproportionate burden of behavioral symptoms, it is less clear whether these symptoms are caused by the hepatitis C infection itself or are the result of characteristics—the conditions and attributes—of the people who are most likely to contract hepatitis C.⁵ Consistent with the first theory—the idea that hepatitis C infection is the cause of these symptoms—are data that show symptom improvement following standard hepatitis C treatment: interferon plus ribavirin. While it is not known how infection with hepatitis C might contribute to behavioral symptoms, converging lines of evidence suggest that the release of inflammatory molecules in the central nervous system may directly cause these symptoms and may also promote these symptoms by affecting neurotransmitters such as serotonin.

Other data support the second theory, suggesting that people with hepatitis C tend to also have psychiatric conditions that cause behavioral symptoms. For example, in studies of subjects with hepatitis C and uninfected control subjects, the differences in neurobehavioral symptoms between these groups are greatly reduced when both sets of subjects are matched to each other in terms of past history of substance abuse and other factors that increase the likelihood of psychiatric illness.⁵

Treatment of Quality of Life Complaints

Whatever the cause of these neurobehavioral symptoms, a critical first step in treat-

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See also references cited in articles in this issue.

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ing them is an accurate assessment of symptoms, and, if indicated, appropriate psychiatric diagnosis. Clinicians can accurately identify the presence of a range of behavioral symptoms through the use of validated self-report questionnaires that can be easily completed by patients. Especially useful in this regard is a standardized and systematic measure for monitoring depression.

Patients with high depressive symptom scores are likely to benefit from antidepressant treatment.⁶ Although not well studied, it is likely that psychotherapy would be as effective in treating depression in patients with hepatitis C as it is in otherwise healthy but depressed people. In patients whose primary complaint is fatigue, psychostimulants, bupropion, and modafinil, may be especially beneficial.⁶ Depressed patients with hepatitis C should also be carefully evaluated for ongoing substance abuse effects that may contribute to—or cause—their symptoms.

Many studies show that people with hepatitis C who achieve a sustained viral response following treatment with interferon plus ribavirin experience overall improvements in quality of life, in general, and fatigue, in particular, when compared to their pretreatment state.³ Thus, in addition to lowering the risk of long-term liver damage, successful hepatitis C treatment has now emerged as a key tool for eradicating the galaxy of neurobehavioral symptoms associated with hepatitis C.

However, in this regard hepatitis C treatment follows the old maxim, “It is always darkest before the dawn.” Treatment, itself, significantly worsens quality of life in most patients, primarily by inducing or worsening all the neurobehavioral symptoms discussed here. Approximately 30 percent to 60 percent of people receiving treatment will develop clinically significant depression, and a higher percentage will suffer from one or more specific neurobehavioral symptoms such as fatigue and insomnia.⁶ In turn, people who develop these symptoms are less likely to tolerate or comply with hepatitis C treatment, increasing their risk for treatment failure, irrespective of other factors that might lead to a poor treatment response.⁷

Antidepressants have been shown to effectively reduce many of the neurobehavioral symptoms associated with hepatitis C treatment.⁶ Clinical experience suggests that other agents useful for alleviating individual symptoms include hypnotics—such as zolpidem, zalciprone, or trazodone—for insomnia, psychostimulants and modafinil for fatigue, and erythropoietin for the anemia that can contribute to fatigue.⁶ Behavioral strategies such as adequate hydration, exercise, and psychotherapy, as well as

general emotional support, are also of great value in helping patients tolerate treatment.

Patients can either take antidepressants prior to starting hepatitis C treatment or begin antidepressants if depressive symptoms emerge during treatment.⁶ The most consistent risk factor for developing significant depression in response to hepatitis C treatment is the presence of even mild depressive symptoms prior to treatment.⁶ Therefore, people with hepatitis C who have depressive symptoms should consider antidepressant pretreatment, and people who have been depressed in the past, even if they do not have current symptoms, should also consider antidepressant pretreatment. Again, a standardized depression rating scale, employed before treatment begins, can be especially valuable in helping clinicians establish an individual's risk of developing depression as a result of hepatitis C treatment.

Clinicians should aggressively treat depressive symptoms in individuals who have not been pretreated with antidepressants, because it is clear from many studies that symptoms are not likely to regress spontaneously once they have emerged. Finally, clinicians should not abruptly withdraw clients from antidepressants following completion of hepatitis C treatment. Rather, these agents should be tapered slowly—over several weeks at least—once an individual has returned to at least their baseline level of emotional functioning.

Conclusion

The goal of improved quality of life has emerged as a central challenge for clinicians working with hepatitis C. Hepatitis C treatment, itself, can both alleviate these symptoms, enhancing quality of life, and induce or worsen them. The good news is that for the majority of people with behavioral symptoms, a variety of techniques can safely and effectively treat the depression, anxiety, and fatigue that may accompany both hepatitis C and its treatment.

Comments and Submissions

We invite readers to send letters responding to articles published in *FOCUS* or dealing with current AIDS research and counseling issues. We also encourage readers to submit article proposals. Send correspondence to rob.marks@ucsf.edu or to Editor, *FOCUS*, UCSF AIDS Health Project, Box 0884, San Francisco, CA 94143-0884.

Recent Reports

Coinfection and HIV Antiviral Therapy

Weis N, Lindhardt BO, Kronborg G, et al. Impact of hepatitis C virus coinfection on response to highly active antiretroviral therapy and outcome in HIV-infected individuals: A nationwide cohort study. *Clinical Infectious Diseases*. 2006; 42(10): 1481–1487. (Hvidovre Hospital, Copenhagen, Denmark.)

As Heather Lusk discusses in her overview article, researchers have consistently found that HIV causes the acceleration of hepatitis C disease progression, but results have not been as consistent regarding the impact of hepatitis C on HIV disease. A Danish study, published this month, found that one way hepatitis C shortens the lives of people with HIV is by compromising their response to HIV antiviral therapy. The following excerpt is adapted from the published abstract and article:

Coinfection with hepatitis C in HIV-infected patients may decrease the effectiveness of HIV antiviral therapy. This prospective cohort study included all adult Danish HIV-1-infected patients who started highly active antiretroviral therapy between January 1, 1995 and January 1, 2004. Patients were classified as hepatitis C-positive (443 patients, or 16 percent of the sample), hepatitis C-negative (2183 patients, or 80 percent of the sample) and hepatitis C-status unknown (108 patients who had never been tested for hepatitis C, or 4 percent of the sample).

Both overall mortality and mortality from liver disease were significantly higher in the hepatitis C-positive group than in the hepatitis C-negative group. Although the researchers observed no difference in HIV viral load between the hepatitis C-positive and hepatitis C-negative groups, the hepatitis C-positive group had a marginally lower absolute CD4+ cell count leading the researchers

to conclude that HIV–hepatitis C coinfecting patients were compromised in their response to HIV antiviral therapy. Subjects with hepatitis C were also more likely to discontinue their HIV antiviral regimens.

Because most of the subjects who were hepatitis C-positive were also injection drug users, the researchers had difficulty differentiating between the effects of hepatitis C and the effects of injection drug use on HIV antiviral efficacy. However, in analyses that excluded injection drug using participants, the hepatitis C-positive group had higher rates of overall mortality and liver-related mortality than the hepatitis C-negative group.

Cognitive Effects of Hepatitis C Infection

Cherner M, Letendre S, Heaton RK, et al. Hepatitis C augments cognitive deficits associated with HIV infection and methamphetamine. *Neurology*. 2005; 64(8): 1343–1347. (University of California, San Diego; and VA San Diego Healthcare System.)

As Charles Raison notes, people with hepatitis C live with a range of neurobehavioral symptoms, including depression, anxiety, fatigue, and cognitive disturbances, all of which impair their quality of life. This San Diego study examined the additive effect of

hepatitis C, HIV, and a history of methamphetamine dependence on cognitive capacities. The following excerpt is adapted from the published abstract:

Researchers examined neurocognitive functioning in 430 study participants who had hepatitis C, HIV, a history of methamphetamine dependence, or combinations of these three risk factors for cognitive deficits, or who were “normal” controls who had none of these risk factors. The study found that rates of both global neu-

ropsychological impairment and specific neuropsychological impairment increased with the number of these risk factors.

Hepatitis C serostatus was a significant predictor of neuropsychological performance both globally and in the specific areas of learning, abstraction, and motor skills. Hepatitis C infection, however, did not predict scores in attention/working

A study of two samples of injection drug users—one from 1990, when New York instituted syringe exchange, and the other from 2001—found that between these two years, HIV prevalence dropped 41 percent and hepatitis C prevalence dropped 27 percent.

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memory or verbal fluency. Researchers concluded that infection with the hepatitis C virus contributes to the neuropsychological deficits observed in HIV-infected and stimulant-dependent populations.

Syringe Exchange Cuts Hepatitis C Prevalence

Des Jarlais DC, Perlis T, Arasteh K, et al. Reductions in hepatitis C virus and HIV infections among injecting drug users in New York City, 1990–2001. *AIDS*. 2005; 19(Suppl. 3): S20–S25. (Beth Israel Medical Center, New York; National Development and Research Institutes, New York; and New York State Department of Health and Mental Hygiene.)

Lusk reports that more than 60 percent of new hepatitis C infections occur in people who inject drugs. This study discusses the association between the expansion of needle exchange and reductions in both HIV and hepatitis C incidence in New York. The following excerpt is adapted from the published abstract:

Between 1990 and 2001, New York experienced a great expansion of syringe exchange: the number of syringes exchanged annually rose from 250,000 to 3,000,000 during that period. Researchers conducted cross-sectional seroprevalence surveys of injection drug users entering drug abuse treatment, with sample sizes for hepatitis C virus of 72 in 1990–1991 and 412 in 2000–2001.

Over the 11-year period, HIV prevalence in this population of injection drug-using subjects declined from 54 percent to 13 percent. Hepatitis C prevalence declined from 80 percent to 59 percent among HIV-negative individuals and from 90 percent to 63 percent overall. The estimated hepatitis C incidence in 2000–2001 among new injectors was 18 per 100 person-years at risk. The large-scale expansion of syringe exchange was temporally associated with large reductions in both HIV and hepatitis C prevalence. The prevalence and incidence of hepatitis C, however, still remain at high levels among injection drug users in New York.

Interferon Treatment and Depression

Laguno M, Blanch J, Murillas J, et al. Depressive symptoms after initiation of interferon therapy in human immunodeficiency virus-infected patients with chronic hepatitis C. *Antiviral Therapy*. 2004; 9(6): 905–909. (Hospital Clinic Universitari de Barcelona, Spain.)

Raison's article explores the complexity of treating hepatitis C infection without causing intolerable levels of depression. This Spanish study found a high incidence of depression in subjects being treated for hepatitis C with interferon, with most subjects responding well to antidepressant therapy. The following excerpt is adapted from the published abstract:

Researchers evaluated the incidence and management of depressive symptoms among people coinfecting with HIV and hepatitis C who began interferon-alpha and ribavirin treatment during the recruitment period from April 2001 to April 2003. The study excluded patients with a history of major depressive disorder.

Of 113 participants who started interferon-alpha therapy during the recruitment period, 45 (40 percent) developed symptoms of depression (including sadness, tiredness, and apathy). Most of the participants (60 percent) showed depressive side effects in the first three months after initiation of interferon-alpha. In addition, during the study, three patients developed psychotic symptoms and one committed suicide.

Most of the depressive symptoms were not severe and improved with antidepressant therapy and without reduction or cessation of interferon-alpha therapy. Of the 45 participants who developed depressive symptoms, 20 (44 percent) were treated with citalopram, a selective serotonin reuptake inhibitor, which resulted in a significant improvement in their symptoms.

The researchers recommend close assessment of psychiatric symptoms during the first weeks after initiating interferon-alpha treatment and early antidepressant treatment to avoid early dropouts from interferon-alpha.

Next Issue

Clients who grapple with serious mental health disorders as well as HIV challenge providers to develop innovative therapeutic interventions. In the July issue of *FOCUS*, **Thomas Lynch, PhD**, Associate Professor of Psychiatry and Behavioral Sciences at Duke University, and **Christopher Kenedi, MD, MPH**, a resident physician at Duke University Medical Center, explore how dialectical behavioral therapy can bridge the gap between therapists and clients who live with HIV and borderline personality disorder. A fusion of cognitive-behavioral and mindfulness approaches, dialectical behavioral therapy offers a fresh perspective.

Also in the July issue, **Mark Winiarski, PhD**, Director of Mental Health Services for the North Bronx Healthcare Network, discusses how researchers and clinicians can develop client-centered treatment models for dually and triply diagnosed clients, particularly clients who also struggle with poverty.